

SEQUENCE LISTING

<110> CO, MAN SUNG

VASQUEZ, MAXIMILIANO

<120> ANTITHROMBOTIC AGENT AND HUMANIZED ANTI-VON WILLEBRAND FACTOR
MONOCLONAL ANTIBODY

<130> 202617US0PCT

<140> 09/763,129

<141> 2001-02-20

<150> PCT/US99/16724

<151> 1999-08-19

<150> 09/136,315

<151> 1998-08-19

<160> 8

<170> PatentIn version 3.1

<210> 1

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<212> DNA

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| Met Asp Phe Gly Leu Ile Phe Phe Ile Val Ala Leu Leu Lys Gly Val | |
| 1 5 10 15 | |
| cag tgt gag gtg aaa ctt ctc gag tct gga ggt ggc ctg gtg cag act | 96 |
| Gln Cys Glu Val Lys Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Thr | |
| 20 25 30 | |
| gga gga tcc ctg aaa ctc tcc tgt gca gcc tca gga ttc gat ttt agt | 144 |
| Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser | |
| 35 40 45 | |
| aga ttc tgg atg agt tgg gtc cgg cag gct cca ggg aaa ggg cta gaa | 192 |
| Arg Phe Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu | |
| 50 55 60 | |
| tgg att gga gaa gtt aat cca gat aac aat acg atg aac tat acg cca | 240 |
| Trp Ile Gly Glu Val Asn Pro Asp Asn Asn Thr Met Asn Tyr Thr Pro | |
| 65 70 75 80 | |
| tct cta aag gat aaa ttc atc atc tcc aga gac aac gcc aaa aat acg | 288 |
| Ser Leu Lys Asp Lys Phe Ile Ile Ser Arg Asp Asn Ala Lys Asn Thr | |
| 85 90 95 | |
| ctg tac ctg caa atg agt caa gtg aga tct gag gac aca gcc ctt tac | 336 |
| Leu Tyr Leu Gln Met Ser Gln Val Arg Ser Glu Asp Thr Ala Leu Tyr | |
| 100 105 110 | |
| tac tgt gca aga cct ccc tac tat ggt agc tac ggg ggg ttt gct tac | 384 |
| Tyr Cys Ala Arg Pro Pro Tyr Tyr Gly Ser Tyr Gly Gly Phe Ala Tyr | |
| 115 120 125 | |
| tgg ggc caa ggg act ctg gtc tct gtc tcg cca | 417 |
| Trp Gly Gln Gly Thr Leu Val Ser Val Ser Pro | |
| 130 135 | |

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Met Asp Phe Gly Leu Ile Phe Phe Ile Val Ala Leu Leu Lys Gly Val
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Gln Cys Glu Val Lys Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Thr
20 25 30

Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser
35 40 45

Arg Phe Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
50 55 60

Trp Ile Gly Glu Val Asn Pro Asp Asn Asn Thr Met Asn Tyr Thr Pro
65 70 75 80

Ser Leu Lys Asp Lys Phe Ile Ile Ser Arg Asp Asn Ala Lys Asn Thr
85 90 95

Leu Tyr Leu Gln Met Ser Gln Val Arg Ser Glu Asp Thr Ala Leu Tyr
100 105 110

Tyr Cys Ala Arg Pro Pro Tyr Tyr Gly Ser Tyr Gly Gly Phe Ala Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Ser Val Ser Pro
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| atg | agt | gtg | ccc | act | cag | gtc | ctg | ggg | ttg | ctg | ctg | ctg | tgg | ctt | aca | 48 |
| Met | Ser | Val | Pro | Thr | Gln | Val | Leu | Gly | Leu | Leu | Leu | Leu | Trp | Leu | Thr | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | |
| | | | | | | | | | | | | | | | | |
| gat | gcc | aga | tgt | gac | atc | cag | atg | act | cag | tct | cca | gcc | tcc | cta | tct | 96 |
| Asp | Ala | Arg | Cys | Asp | Ile | Gln | Met | Thr | Gln | Ser | Pro | Ala | Ser | Leu | Ser | |
| | | | 20 | | | | | 25 | | | | | 30 | | | |
| | | | | | | | | | | | | | | | | |
| gta | tct | gtg | gga | gaa | act | gtc | acc | atc | aca | tgt | cga | gca | agt | gag | aat | 144 |
| Val | Ser | Val | Gly | Glu | Thr | Val | Thr | Ile | Thr | Cys | Arg | Ala | Ser | Glu | Asn | |
| | | 35 | | | | | 40 | | | | | 45 | | | | |
| | | | | | | | | | | | | | | | | |
| att | tac | aat | aat | tta | gct | tgg | tat | cag | cag | aga | cag | gga | aaa | tct | cct | 192 |
| Ile | Tyr | Asn | Asn | Leu | Ala | Trp | Tyr | Gln | Gln | Arg | Gln | Gly | Lys | Ser | Pro | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |
| | | | | | | | | | | | | | | | | |
| cag | ctc | ctg | gtc | tat | gct | gca | aca | aac | tta | gca | gat | ggg | gtg | cca | tca | 240 |
| Gln | Leu | Leu | Val | Tyr | Ala | Ala | Thr | Asn | Leu | Ala | Asp | Gly | Val | Pro | Ser | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | |
| | | | | | | | | | | | | | | | | |
| agg | ttc | agt | ggc | agt | gga | tca | ggc | aca | cag | tat | tcc | ctc | aag | atc | gac | 288 |
| Arg | Phe | Ser | Gly | Ser | Gly | Ser | Gly | Thr | Gln | Tyr | Ser | Leu | Lys | Ile | Asp | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| | | | | | | | | | | | | | | | | |
| agc | ctg | cag | tct | gaa | gat | ttt | ggg | agt | tat | tac | tgt | caa | cat | ttg | tgg | 336 |
| Ser | Leu | Gln | Ser | Glu | Asp | Phe | Gly | Ser | Tyr | Tyr | Cys | Gln | His | Leu | Trp | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |
| | | | | | | | | | | | | | | | | |
| act | tct | ccg | tac | acg | ttc | gga | ggg | ggg | acc | aag | ctg | gaa | ata | aaa | | 381 |
| Thr | Ser | Pro | Tyr | Thr | Phe | Gly | Gly | Gly | Thr | Lys | Leu | Glu | Ile | Lys | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | |

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Met Ser Val Pro Thr Gln Val Leu Gly Leu Leu Leu Leu Trp Leu Thr
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Asp Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser
 20 25 30

Val Ser Val Gly Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn
 35 40 45

Ile Tyr Asn Asn Leu Ala Trp Tyr Gln Gln Arg Gln Gly Lys Ser Pro
 50 55 60

Gln Leu Leu Val Tyr Ala Ala Thr Asn Leu Ala Asp Gly Val Pro Ser
 65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asp
 85 90 95

Ser Leu Gln Ser Glu Asp Phe Gly Ser Tyr Tyr Cys Gln His Leu Trp
 100 105 110

Thr Ser Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
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| Met | Asp | Phe | Gly | Leu | Ile | Phe | Phe | Ile | Val | Ala | Leu | Leu | Lys | Gly | Val | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| cag | tgt | gag | gtg | caa | ctt | gtc | gag | tct | gga | ggt | gga | cta | gtg | cag | cct | 96 |
| Gln | Cys | Glu | Val | Gln | Leu | Val | Glu | Ser | Gly | Gly | Gly | Leu | Val | Gln | Pro | |
| | | | 20 | | | | | 25 | | | | | 30 | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| gga | gga | tca | ctg | aga | ctc | tcc | tgt | gca | gcc | tca | gga | ttc | gat | ttt | agt | 144 |
| Gly | Gly | Ser | Leu | Arg | Leu | Ser | Cys | Ala | Ala | Ser | Gly | Phe | Asp | Phe | Ser | |
| | | 35 | | | | | 40 | | | | | 45 | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| aga | ttc | tgg | atg | agt | tgg | gtc | cgg | cag | gct | cca | ggg | aaa | ggg | ctc | gag | 192 |
| Arg | Phe | Trp | Met | Ser | Trp | Val | Arg | Gln | Ala | Pro | Gly | Lys | Gly | Leu | Glu | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| tgg | att | gga | gaa | gtt | aat | cca | gat | aac | aat | acg | atg | aac | tat | acg | cca | 240 |
| Trp | Ile | Gly | Glu | Val | Asn | Pro | Asp | Asn | Asn | Thr | Met | Asn | Tyr | Thr | Pro | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| tct | cta | aag | gat | aaa | ttc | acc | atc | tcc | aga | gac | aac | gcc | aaa | aat | acg | 288 |
| Ser | Leu | Lys | Asp | Lys | Phe | Thr | Ile | Ser | Arg | Asp | Asn | Ala | Lys | Asn | Thr | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| ctg | tac | ctg | caa | atg | aac | tca | ttg | aga | gct | gag | gac | acg | gcc | gtt | tac | 336 |
| Leu | Tyr | Leu | Gln | Met | Asn | Ser | Leu | Arg | Ala | Glu | Asp | Thr | Ala | Val | Tyr | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| tac | tgt | gca | aga | cct | ccc | tac | tat | ggt | agc | tac | ggg | ggg | ttt | gct | tac | 384 |
| Tyr | Cys | Ala | Arg | Pro | Pro | Tyr | Tyr | Gly | Ser | Tyr | Gly | Gly | Phe | Ala | Tyr | |
| | | 115 | | | | | 120 | | | | | 125 | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|--|--|-----|
| tgg | ggc | caa | ggg | act | ctg | gtc | acc | gtc | tcc | tca | | | | | | 417 |
| Trp | Gly | Gln | Gly | Thr | Leu | Val | Thr | Val | Ser | Ser | | | | | | |
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Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
20 25 30

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser
35 40 45

Arg Phe Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
50 55 60

Trp Ile Gly Glu Val Asn Pro Asp Asn Asn Thr Met Asn Tyr Thr Pro
65 70 75 80

Ser Leu Lys Asp Lys Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr
85 90 95

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
100 105 110

Tyr Cys Ala Arg Pro Pro Tyr Tyr Gly Ser Tyr Gly Gly Phe Ala Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
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<222> (1)..(381)

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<400> 7

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| Met Ser Val Pro Thr Gln Val Leu Gly Leu Leu Leu Leu Trp Leu Thr | |
| 1 5 10 15 | |
| gat gcc aga tgt gac atc cag atg act cag tct cca tcc tcc cta tct | 96 |
| Asp Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser | |
| 20 25 30 | |
| gca tct gtg gga gac agg gtc acc atc aca tgt cga gca agt gag aat | 144 |
| Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn | |
| 35 40 45 | |
| att tac aat aat tta gct tgg tat cag cag aaa ccg gga aaa gct cct | 192 |
| Ile Tyr Asn Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro | |
| 50 55 60 | |
| aag cta cta gtc tat gct gca aca aac tta gca gat ggt gtg cca tca | 240 |
| Lys Leu Leu Val Tyr Ala Ala Thr Asn Leu Ala Asp Gly Val Pro Ser | |
| 65 70 75 80 | |
| agg ttc agt ggc agt gga tca ggc aca cag tat acc ctc acg atc agc | 288 |
| Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Tyr Thr Leu Thr Ile Ser | |
| 85 90 95 | |
| agc ctc cag cct gag gat ttt gcg act tat tac tgt caa cat ttg tgg | 336 |
| Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Leu Trp | |
| 100 105 110 | |
| act tct ccg tac acg ttc gga ggg ggg acc aag gtg gaa ata aaa | 381 |
| Thr Ser Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys | |
| 115 120 125 | |

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Met Ser Val Pro Thr Gln Val Leu Gly Leu Leu Leu Trp Leu Thr
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Asp Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn
35 40 45

Ile Tyr Asn Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
50 55 60

Lys Leu Leu Val Tyr Ala Ala Thr Asn Leu Ala Asp Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Tyr Thr Leu Thr Ile Ser
85 90 95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Leu Trp
100 105 110

Thr Ser Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
115 120 125